THE HEALTH CARE BIOTECHNOLOGY INDUSTRY IN FRANCE
LEEM HEALTH CARE BIOTECHNOLOGY COMMITTEE REPORT
ISSUE 2014
Study perimeter

- **BIOTECHNOLOGY OECD DEFINITION**
  “The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.”

- **TARGETS**: SME and micro-enterprises

- **FIELD OF APPLICATIONS**: Human and animal health

- **ACTIVITIES**: > 25% in biotechnology / R&D, production and/or commercialisation of products (therapeutic products and products to conduct research) and/or services dedicated to health care industries, such as CRO (Contract Research Organisation). Equipment manufacturers are not included in this study.

- **APPLICATIONS**: Beyond therapeutic products, *In Vitro* Diagnostic and Medical Devices are included, provided the products include biotechnologies.
A growing sector

• HEALTH CARE BIOTECHNOLOGY SECTOR IN FRANCE: 457 companies in 2013 versus 388 in 2010, without the 64 big pharma or diagnostic companies

Distribution of health care biotechnology companies (without big pharma) by company size (n=457)

- 55% Non-SME (250-4999)
- 33% SME (>50)
- 8% SME (<50)
- 4% Micro-enterprises (<10)

- 18% growth regarding the number of companies
- Mainly micro-enterprises in this sector
- Turnover of € 2.8 billion
- 33,000 employees
- 95% in human health
Companies are located in pharmaceutical historical regions. They focus mainly on oncology and infectiology.

Geographical distribution of health care biotechnology companies (n=457)

Companies focus area by indication (n=231, companies developing products)*

Therapeutic areas involving less than 3% of the companies are not represented.
Companies along the value chain (n=457)

- 231 companies developing products
- 84 dual companies: products and services
- 142 companies providing services

Of which « Therapeutic products » (230 companies)
Of which « Diagnostic products » (83 companies)
Of which « Products to conduct research » (87 companies)
Evolution of companies’ positioning since 2010

- **231 companies developing products**: 210 in 2010
  - Of which « Therapeutic products » (230 companies)
  - Of which « Diagnostic products » (83 companies)
  - Of which « Products to conduct research » (87 companies)

- **84 dual companies: products and services**: 23 in 2010

- **142 companies providing services**: 155 in 2010
  - CRO (188 companies) 138 in 2010
  - CMO (21 companies) 20 in 2010
  - Bioinformatics (29 companies) 12 in 2010

**Growth rate (%)**
- Global: 18
- Products companies: 10
- Services companies: -8
- Dual companies: 265
- CRO: 37
- CMO: 5
- Bioinformatics: 142

→ Evolution of the companies positioning towards dual model
Since 2010, several companies moved towards a dual model

**Product to dual:**
- Generating sales
- Securing the overall financing plan
- Strengthening the technology awareness through service before embedding it in a product

**Service to dual:**
- Generating growth and value
- More relevant and readable for fundraising from venture capitalists
- Targeted market: therapeutic products (85%)

**Complex model to manage**
- Evolution to monitor in the coming years
Sector dynamics since 2010

- **46 COMPANIES OUT OF BUSINESS**
  - Mainly micro-enterprises and SME (<50 employees)

- **72 CREATED COMPANIES**
  - Interest for the dual model (25%)

- **23 COMPANIES NOT INVOLVED IN HEALTH ANYMORE**
  - Shifting to ‘cleantech’, nutrition or cosmetics

- **66 COMPANIES INCLUDED IN THE SCOPE**
  - Investment in the health sector more explicit or reaching a threshold of visibility since 2010
Focus on disappeared companies

- **46 COMPANIES OUT OF BUSINESS SINCE 2010, 12%**
  - Majority (32) → development issues for companies
  - 13 acquisitions and consolidations (ex: Millegen via LFB), of which 85% were realised by French companies (11/13)

- **NO SIGNIFICANT OVERREPRESENTATION OF ONE CLASS OF COMPANIES**
  (PRODUCT/DUAL/SERVICE)

<table>
<thead>
<tr>
<th></th>
<th>Total companies from the 2010 database (%)</th>
<th>Disappeared companies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product</td>
<td>54</td>
<td>50</td>
</tr>
<tr>
<td>Service</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>Dual</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>

- **AMONG THE 49 IN VITRO DIAGNOSTICS IDENTIFIED IN 2010, 13 HAVE DISAPPEARED, 27%**.
  - They thus represent 28% of disappearances while they represented 13% of companies
Companies are struggling to grow

- **LOOKING AT CRO (188 COMPANIES)**
  - 57% of these firms have less than 10 employees
  - 161 companies generate sales, among them 83% generate less than €2 millions
  - In this population, the turnover/staff ratio is €46,848, (still turnover represents only part of a company’s revenues)
  - If limiting to companies older than 3 year old, the ratio is €49,318

- **DIFFICULTIES RELATED TO SEVERAL FACTORS**
  - Funding
  - International competition (Eastern Europe, Asia, ...)
  - National competition from public structures (platforms, institutes, Equipex, CRT, ...), in particular on preclinical activities, enhanced by the fact that all expenditure contracted out to public-sector bodies is double-counted
  - Lack of offers consolidation, at the creation stage or during companies lifecycle
A lack of funding in the post-creation stages

**Creation**
- 1€  
  - 1st round
  - Business Angels
  - Crowdfunding
  - Seed Fund (reinforced by FNA since 2011)
  - Bpifrance
  - Grants

**« Death valleys »**
- 10€  
  - 2nd round
  - European Investment fund
  - ETI 2020
  - Regional Investment fund

**Development**
- 20€  
  - 3rd round
  - Strategic Investment Fund
  - IPO

**Post-creation funding**
- Innobio funds
- Large Venture (Bpifrance)

Available funding

Financing needs

**Research Tax Credit (CIR); Innovation tax credit (CII); Competitiveness and Employment Tax Credit (CICE)**

Public funding to projects: ANR, FUI, PSPC, PIA, Horizon 2020, Instrument PME, Bpifrance, ...

“Young Innovative Company “ label
French stock market dynamism

- **26 PUBLIC COMPANIES IN THE SCOPE**
  - Capitalisation: € 6 billion (May 2014)

- **AMOUNT OF CAPITALISATION AND FUND RAISED IS AN ORDER OF MAGNITUDE LOWER THAN IN USA OR UK**
  - Circassia, € 300M raised in March 2014 (UK)
  - Ultragenyx pharmaceuticals, € 90M raised in January 2014 (USA)

- **KEY ISSUE OF CRITICAL MASS**
  - Economic efficiency, profitability
  - Sufficient visibility
  - Necessary consolidation

- **DIFFICULTIES IN RAISING FUNDS DURING THE DEVELOPMENT PHASE**
Numerous Public-Private collaborations

- 46% of survey respondents indicate having partnerships
  - Academic environment favorable for collaborations
    - France well positioned (2nd to 4th place in international rankings, depending on the life sciences field)
    - Research of excellence supported by the PIA (Labex, etc)
    - Good integration between academic research and hospital: 32 CHRU, 6 IHU and 2 PHU
    - Leader in the fields of cancer and rare diseases in clinical research
  - Structures focused on collaborative research
    - Recent structures dedicated to collaborations (IRT, LabCom, Instituts Carnot)

- FUI and BPIFRANCE fund a large share of these partnerships
  - 38% participation in an FUI funded project (survey respondents)
  - 40% of ISI collaborative funding (Innovation Stratégique Industrielle, Bpifrance) dedicated to health
Smaller Private-Private collaborations

- COLLABORATIONS ALL ALONG THE VALUE CHAIN
- NEW FORMS OF PARTNERSHIPS EMERGING
  - Business centers
  - Staff secondments

- BUT MODEST FINANCIAL AGREEMENTS IN FRANCE

<table>
<thead>
<tr>
<th></th>
<th>Total amount</th>
<th>Upfront payment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>International</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roche – Chiamsa</td>
<td>€ 430M</td>
<td>€ 47M</td>
</tr>
<tr>
<td>Ablynx - AbbVie</td>
<td>€ 607.7M</td>
<td>€ 126.6M</td>
</tr>
<tr>
<td>MorphoSys - GSK</td>
<td>€ 420M</td>
<td>€ 20M</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BioAlliance Pharma - Innocutis</td>
<td>€ 3.6M</td>
<td>NC</td>
</tr>
<tr>
<td>DBV - Stallergenes</td>
<td>€ 145M</td>
<td>NC</td>
</tr>
<tr>
<td>Cellectis - Servier</td>
<td>€ 618M (6 products)</td>
<td>€ 7M</td>
</tr>
</tbody>
</table>

12 Mai 2014
Support to be strengthen during the development phase

- **28 INCUBATORS WITH THE « ALLÈGRE » LABEL**
  - 28% of incubated projects in life sciences
  - 3,4% in the biotechnology field

- **34% OF MESR CONTEST WINNERS ARE IN THE PHARMA INDUSTRY / BIOTECH SECTOR**

- **€ 2.7 billion FINANCIAL SUPPORT FOR COMPANY CREATION IN 2011**
  - Large collection of support tools making them difficult to understand

- **SUPPORT DURING THE DEVELOPMENT PHASE IS MORE LIMITED**
  - With the exception of some initiatives (BPI Biotech Garantie)
  - French Cour des Comptes « Evaluation of measures to support entrepreneurship » 2012
Biotech sector dominated by SMEs

3rd position in terms of number of companies ➔ Dominated by SMEs with less than 250 employees
United States largely dominates in terms of turnover

**Turnover (€ billion)**

- 0.6
- 1.1
- 2.4
- 2.8
- 3.4
- 4.1
- 5.1
- 6.1
- 6.7
- 7
- 46.2

**7th position in terms of turnover at European level**

**Ratio turnover / employees (k€)**

- 85
- 100
- 145
- 190
- 194
- 253
- 268
- 389
- 461
- 721
- 999

**11th position in terms of turnover / staff ratio**
Number of therapeutic products under development (bioproducts and small molecules)

4th position at European level in terms of number of therapeutic products under development → 49% in preclinical, 12% in phase I, 26% in phase II and 13% in phase III → Stable proportions for France and Europe for a few years

Main therapeutic areas: oncology, infectious disease and neurology, main biotech areas in concordance with WHO and H2020
France slightly behind on private funding

- Fundraising dominated by UK and DE at European level

- 4th position of France in terms of venture capital collected and 6th position for total private funds raised at the European level

2012 data E&Y
Despite low capitalisations, French stock exchange is dynamic

• France dominates in terms of number of public companies
  
  Both for long periods (27 introductions between 2007 and 2012), and recently (4 on T1 2014)

• BUT…ranks 5th in terms of capitalisation per company at the European level

<table>
<thead>
<tr>
<th>Country</th>
<th>Capitalisation (€ billion)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>8,3</td>
</tr>
<tr>
<td>Belgium</td>
<td>2,2</td>
</tr>
<tr>
<td>Denmark</td>
<td>2,8</td>
</tr>
<tr>
<td>Spain</td>
<td>0,08</td>
</tr>
<tr>
<td>France</td>
<td>6,1</td>
</tr>
<tr>
<td>Israel</td>
<td>1</td>
</tr>
<tr>
<td>Italy</td>
<td>0,17</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1,9</td>
</tr>
<tr>
<td>Sweden</td>
<td>2,4</td>
</tr>
<tr>
<td>Switzerland</td>
<td>17,2</td>
</tr>
<tr>
<td>United States</td>
<td>262</td>
</tr>
</tbody>
</table>

Zone Bourse
Identified areas of improvement

Financing company development (Death Valley) and attracting private capital, particularly foreign capital

The difficulties faced by public-private partnerships in establishing a mutual understanding of how to achieve common goals and appropriate milestones and/or deliverables

Business growth and acquisition (the consolidation of companies in the sector is not yet taking place)

The need to strengthen the international mindset among biotechnology companies
Examples of international measures

Bon CTI
→ Assistance to partner search within research institutes and funding of collaborations

Bayern Innovativ
→ Technical Centre organising events with all actors

Links between academic and private worlds throughout people’s careers

Biomedical Catalyst Fund in translational medicine: 3 prices supporting projects from idea to marketing (death valley)

Support for the identification and remuneration of high value company managers (CEO, CFO, CSO, COO, CIO)

4 areas of improvement in France

International mindset

Financing

Collaborations

Growth

AWEX thematic network